REMARKS

Applicants acknowledge their election of claims 56-71 for prosecution on the merits. Applicants also note the Examiner's objection to the wording of claim 67. Applicants have corrected that claim by inserting the omitted word "that" at line 6 thereof. New independent claim 72 has been added; claim 72 is directed to the same invention as the other elected claims.

Response to Rejections under 35 USC §112, ¶1

In the Office Action, the Examiner rejected claims 57, 66, and 67 under 35 USC §112, ¶1 as non-enabling. Specifically, the Examiner interpreted those claims as encompassing removal of necrotic tissue by the active agent even though the active agent and necrotic tissue never come into contact with each other (Action, p. 3; "[the claims] do not require that the necrotic tissues have any structural, functional, or proximal relationship to the site of contact"). Applicants have now amended claims 57, 66, and 67 so that it is clear that the area of skin placed into contact with the topical preparation containing the active agent includes necrotic tissues. Basis for this amendment is found in the specification for example at page 3, lines 13-15; page 15, lines 9-14; and page 19, lines 10-16.

As an additional basis for rejection, the Examiner asserted at page 4 that, "the claims are problematic in that the person of ordinary skill in the art would not have a reasonable expectation that any given active agent would remove necrotic tissue even if applied directly thereto." The Examiner further asserted that even if "active agent" were interpreted as "enzyme," there would still be no reasonable expectation of success. Applicants note that independent claim 56 has now been amended to recite that the "active agent" comprises "a protein or enzyme." This is in accordance with the definition provided in the specification at page 6, lines 1-2.

Applicants disagree with the Examiner's interpretation of the claims. The claims do not recite that "any" active agent will remove necrotic tissues. Rather, claims 57, 66, and 67 recite that the "active agent" (now recited to be a protein or enzyme) "is selected such that said active agent removes necrotic tissues upon release from said silicone matrix." Thus, persons of skill in the art are directed to "select" as suitable those proteins or enzymes which will function to remove necrotic tissues. Applicants' specification provides substantial guidance in such a

selection by listing numerous enzymes, including protease enzymes, that are known to be effective as debriding agents for necrotic tissues. Further, it is known in this art that certain broad classes of enzymes act as debriding agents for dead or diseased tissue.

In order to establish a basis for rejecting claims for alleged lack of enablement, the Examiner has the initial burden to establish a reasonable basis to question the objective statements of enablement found in an applicant's specification. MPEP §2164.04. The Examiner's first stated reason, that the claims are open to encompassing "any" active agent, is simply wrong and a mischaracterization of the explicit wording of the claims. The second stated reason, that applicants have provided only a "narrow working embodiment," provides no basis for questioning the many other broad statements of operability found in the specification. Applicants are not claiming novel active agents such as proteins or enzymes, but rather are claiming a method of providing an active agent to a site on a patient's skin using controlled release of the active agent from a silicone matrix. The proteins and enzymes have known properties in this art. The Examiner has failed to present any evidence or reasoning that would call into question the truth of any statements made in the specification concerning the claimed invention. Applicants have provided several examples that demonstrate the controlled release of active agents from a silicone matrix. Applicants have amply demonstrated the enablement of the claimed subject matter.

In the Office Action, the Examiner rejected claims 59-61 under 35 USC §112, ¶1 as being non-enabled. The Examiner repeated her assertion that the claims were "problematic in that the person of ordinary skill in the art would not have a reasonable expectation that any given active agent" would perform the recited functions of sterilizing a wound, preventing infection, or accelerating wound healing. Again, the Examiner has mischaracterized the explicit language of the claims. Claims 59-61 recite that the "active agent" (now defined as a protein or enzyme) is "selected such that the active agent" performs the stated function in the claims. Again, applicants have provided an extensive list of known proteins and enzymes having known properties that would result in wound sterilization, infection prevention, or accelerated healing. Applicants submit that one skilled in this art would have sufficient knowledge and skill to make a selection of active agents to perform the functions recited in claims 59-61.

The Examiner opines that the specification "provides no guidance" in the selection of suitable enzymes. However, "a patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). One skilled in this art would have an understanding of which of the many listed proteins and enzymes would have the properties needed to provide the recited functions of wound sterilization, infection prevention, and accelerated healing.

Also in the Office Action, the Examiner rejected claims 57-61, 66, and 67 under 35 USC §112, ¶1 as failing to comply with the written description requirement. Specifically, the Examiner has asserted, page 7, that applicants are claiming subject matter "which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors ...had possession of the claimed invention." Applicants do not understand the rejection to be that statements found in the specification are not commensurate in scope with the claimed subject matter. In fact, statements found in the specification do provide notice that applicants were in possession of the subject matter being claimed.

The Examiner asserts, page 8, that the claims are "broadly drawn to compositions." That statement is clearly in error as the claims are all drawn to methods of providing the release of an active agent topically from a silicone matrix. The Examiner opines (again page 8) that the specification provides "no criteria" or guidance for selecting those active agents which perform the recited functions and would require "undue experimentation." However, such complaints are directed to lack of enablement, not that applicants have not described their invention. As discussed in detail above, applicants have provided an extensive listing of known proteins and enzymes which are suitable for controlled release from the silicone matrix when used to practice the methods of the claimed invention. Applicants need not explain to those skilled in the art what they already know.

The Examiner's discussion, which extends over many pages, mistakenly presumes that applicants are describing and claiming novel proteins and enzymes; they are not. The proteins and enzymes described in the specification are known and possess properties that are also known. The Examiner relies on case law that relates to inadequate description of novel and complex bio-molecules. To the contrary, applicants are not claiming novel bio-molecules. Applicants are claiming novel methods of controllably releasing known enzymes and proteins

from a silicone matrix. The Examiner's arguments and citations to case law on written description are inapposite.

Response to Rejections under 35 USC §112, ¶2

In the Office Action, the Examiner rejected claims 56-67 under 35 USC §112, ¶2, as indefinite in the recitation of the term "active agent." The Examiner asserted (page 11) that the term has "multiple meanings in the art." Applicants disagree. As noted by the Examiner, applicants' specification recites at page 6, lines 1-2 that the term "active agent" shall be understood as referring to proteins, and in particular, enzymes." While applicants believe that such provides an explicit and clear definition for the claim terminology, applicants have amended independent claim 56 to recite that the "active agent" comprises a protein or enzyme. Applicants believe that such amendment is responsive to the rejection and to the Examiner's suggestion. The claims as amended are believed to be clear, definite, and in compliance with §112.

In the Office Action, the Examiner made several other objections to the wording of the claims. Claims 57-61 were objectionable in reciting the conditional "may." Applicants have amended those claims to remove the objectionable terminology. Claim 57 has been amended to provide explicit antecedent basis for the term "necrotic tissues." Claim 59 has been amended as suggested to recite that the active agent sterilizes the wound. Claim 60 has been amended to recite that the active agent generates peroxide, peracid, or activated oxygen species to provide anti-infection properties. Basis for the amended language is found in the specification at page 15, lines 9-14.

The language of claim 61 is believed to be clear and definite as amended. Applicants see no need to specify the degree to which healing is accelerated. Applicants submit that one skilled in the art, after reading applicants' specification, would have a clear and definite understanding of the subject matter being claimed in claim 61.

Claims 62-65 have been objected to as "incomplete" in omitting elements that are essential to the invention described in the specification. Claim 62 recites that the "silicone matrix is selected to have a cross-link density suitable for providing a desired rate of active agent release." As taught in the specification at page 18, lines 12-15, a silicone matrix having a low

cross-link density will provide a faster active agent release rate than a silicone matrix having a high cross-link density. One skilled in the art, after having read applicants' specification, would have a clear and definite understanding of the subject matter claimed in claim 62 (as amended to eliminate the conditional language). There are no essential elements missing from the claim, there are no missing steps, and there are no cooperative relationships that are missing. The claim language recites that there is a relationship between cross-link density and active agent release from the silicone matrix. Nothing more is required to comply with §112, ¶2.

Likewise, claims 63-65 are also believed to be complete as written. The specification, at page 18, lines 5-20, describes the relationships between the features recited in those claims. One skilled in the art, having read applicants' specification, would have a clear and definite understanding of the claimed subject matter. There are no essential elements missing from the claims, there are no missing steps, and there are no cooperative relationships that are missing. The language in each claim recites that there is a relationship between a recited parameter and active agent release from the silicone matrix. The specification explains what those relationships are. Nothing more is required to comply with §112, ¶2.

Claim 66 was rejected under 35 USC §112, ¶2 as containing the conditional language "may." Applicants have amended claim 66 to obviate that problem. Claims 66 and 67 have also been amended to provide explicit antecedent basis for the term "necrotic tissues."

Claim 67 was rejected under 35 USC §112, ¶2 as being incomplete. The Examiner asserted that the "omitted element" was a "correlation between choice of second active agent and inhibition of the first active agent." Applicants disagree. All necessary claim elements are recited including the first and second active agents and how each agent functions. Applicants' specification in the paragraph bridging pages 19-20 clearly explains the relationship between the first and second active agents and provides guidance in their selection.

Claim 67 was also rejected on the basis that the term "around" was indefinite. Applicants submit that the meaning of that term is clear from the specification in the paragraph bridging pages 19-20. The term has its dictionary meaning of extending on all sides. Claim 67 was also rejected because of asserted lack of clarity in the use of the term "topical preparation." Claim 67 has now been amended to clarify the references to the first and second topical preparations. Claim 67 was also rejected because of asserted lack of clarity in the term "second active agent."

Claim 67 has now been amended to recite that the second active agent comprises either a protein or enzyme. Applicants submit that the claim as amended is in compliance with s112.

In the Office Action, the Examiner rejected claim 71 as "confusing" in the recitation of "an abbreviation or symbol." The designation "LG12" for a particular strain of a protease enzyme is believed to be definite and clear. Applicants' specification at page 14, line 20, incorporates by reference the entirety of U.S. Patent No. 5,677,163. That patent describes the strain and names it "LG12." Thus, the designation is not an "abbreviation or symbol," it is the name given to that particular strain of enzyme. Applicants submit that persons skilled in this art would have a clear and definite understanding of the claimed subject matter.

Response to the Prior Art Rejections

Also in the Office Action, the Examiner rejected claims 56-65 under 35 USC §102 as anticipated by Pfister et al (US 5232702). Pfister teaches a silicone pressure sensitive adhesive used in a transdermal drug delivery device. The Examiner asserted that Pfister teaches silicone emulsions comprising a silicone phase and an organic phase dispersed within the silicone phase. The Examiner did not explicitly allege that Pfister teaches that the internal organic phase includes at least one hydrophilic carrier and at least one active agent as recited in claim 56. Applicants assume that the Examiner has interpreted the claimed "active agent" broadly, as was done with respect to the formal rejections made pursuant to §112.

Applicants have amended claim 56 to specify that the claimed "active agent" comprises a protein or enzyme. As understood, Pfister, while broadly describing the incorporation of "drugs, co-solvents, enhancers, and excipients" in the device, does not teach or suggest the use of any active agents comprising proteins or enzymes. Additionally, claims 57-65 have been amended to more clearly recite additional features of the claimed method. Pfister does not teach or suggest the use of any active agents having the properties recited in claims 57-61. Nor does Pfister teach or suggest selecting the silicone matrix or components thereof to accomplish the stated purposes recited in claims 62-65. Accordingly, as Pfister neither teaches nor suggests the subject matter of claims 56-65 as amended, applicants submit that the rejection is not well taken and should be withdrawn.

Also in the Office Action, the Examiner rejected claims 56-65 under 35 USC §102 as anticipated by Powell et al (US 6060546). Powell is directed to non-aqueous silicone emulsions. The Examiner asserted that Powell teaches silicone emulsions comprising a silicone phase and an organic phase dispersed within the silicone phase. The Examiner did not explicitly allege that Pfister teaches that the internal organic phase includes at least one hydrophilic carrier and at least one active agent as recited in claim 56. Applicants assume that the Examiner has interpreted the claimed "active agent" broadly, as was done with respect to the formal rejections made pursuant to §112.

Independent claim 56 has been amended to recite that the internal phase includes three components, namely at least one hydrophilic carrier, at least one hydrophilic component, and at least one active agent. Powell is directed to a non-aqueous emulsion in which the organic liquid forms an internal phase in the continuous silicone phase. The active agents used by Powell are found in the organic liquid. Powell does not teach or suggest a three-component internal phase. Accordingly, the rejection for anticipation is now moot and should be withdrawn.

Also in the Office Action, the Examiner rejected claims 56-65 and 68-71 under 35 USC §103 as unpatentable over either Pfister or Powell. From the Examiner's statements at pages 19-22 of the Office Action, it is apparent that the Examiner is simply repeating the reasoning used with respect to the rejections under §102 based on Pfister and Powell, and then alleging that anything not specifically taught by either reference represents an obvious modification.

As discussed above, the amended claims are not anticipated by either Pfister or Powell. Pfister, while broadly describing the incorporation of "drugs, co-solvents, enhancers, and excipients" in the device, does not teach or suggest the use of any active agents comprising proteins or enzymes. The Examiner has provided no evidence or factual basis for her assertion that the selection of a protein or enzyme as an active agent would have been a "routine matter of optimization." Nothing in Pfister teaches or suggests the use of proteins or enzymes as active agents in a method as claimed. Additionally, claims 57-65 have been amended to more clearly recite additional features of the claimed method. Pfister does not teach or suggest the use of any active agents having the properties recited in claims 57-61. Nor does Pfister teach or suggest selecting the silicone matrix or components thereof to accomplish the stated purposes recited in claims 62-65. Accordingly, as Pfister neither teaches nor suggests the subject matter of claims

56-65 as amended, applicants submit that the obviousness rejection as it relates to Pfister is not well taken and should be withdrawn.

Also as discussed above, independent claim 56 has been amended to recite that the internal phase includes three components, namely at least one hydrophilic carrier, at least one hydrophilic component, and at least one active agent. Powell is directed to a non-aqueous emulsion in which the organic liquid forms an internal phase in the continuous silicone phase. The active agents used by Powell are found in the organic liquid. Powell does not teach or suggest a three-component internal phase. Accordingly, the rejection for obviousness should be withdrawn.

Applicants note that claims 66 and 67 were not rejected on prior art grounds. Applicants submit that new independent claim 72 also is not anticipated by or rendered unpatentable over either of Pfister or Powell.

Response to the Obviousness-Type Double Patenting Rejection

Also in the Office Action, the Examiner provisionally rejected claims 56-65 and 68-71 on the ground of obviousness-type double patenting over claims in co-pending and commonly-owned application Serial No. 10/385,213. The Examiner asserted (page 23) that while the claims were not identical, "they are patentably indistinct from each other." Applicants submit that the Examiner is prohibited from making this rejection.

In Serial No. 10/385,213, in an Office Action mailed December 14, 2004, the Examiner then in charge of that application required restriction from among three groupings. Applicants responded by electing to prosecute the composition claims, claims 1-41, identified as Group I. Claims 55-64, drawn to a method for providing an active agent to the skin were not elected and were eventually canceled. Applicants believe that original claims 56-65 of the present application are identical to non-elected claims 55-64 which were subject to restriction in the parent application. Pursuant to 35 USC §121, this rejection is prohibited. See also, MPEP §804.01. Applicants respectfully request withdrawal of this ground of rejection.

For all of the above reasons, applicants submit that claims 56-72, as amended, are patentable over the cited and applied prior art and are in compliance with §112. Early notification of allowable subject matter is respectfully solicited.

Respectfully submitted,

DINSMORE & SHOHL LLP

By _____

Timothy W. Hagan
Registration No. 29,001

One Dayton Centre
One South Main Street, Suite 1300
Dayton, Ohio 45402-2023
(937) 449-6400
Facsimile: (937) 449-6405
E-mail: tim.hagan@dinslaw.com
TWH/